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Biotech-Chem Library

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TO: Alton Pryor
Location:
Art Unit: 1616
August 18, 2004

if @ 4/6

Case Serial Number: 09/328742

From: P. Sheppard
Location: Remsen Building
Phone: (571) 272-2529

sheppard@uspto.gov

Search Notes

=> fil hcaplus
 FILE 'HCAPLUS' ENTERED AT 09:46:48 ON 18 AUG 2004
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FILE COVERS 1907 - 18 Aug 2004 VOL 141 ISS 8
 FILE LAST UPDATED: 17 Aug 2004 (20040817/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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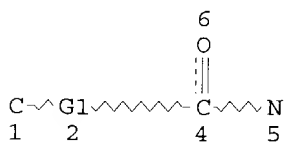
=> d stat que
 L1 STR

C=C
 1 2

NODE ATTRIBUTES:
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 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 2

STEREO ATTRIBUTES: NONE
 L2 SCR 2039 OR 2041 OR 2050 OR 2049 OR 2048 OR 2053 OR 2052 O
 R 2051 OR 2043
 L3 STR



REP G1=(10-20) C
 NODE ATTRIBUTES:
 NSPEC IS RC AT 5
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 5

STEREO ATTRIBUTES: NONE

L4 12044 SEA FILE=REGISTRY SSS FUL (L3 AND L1) NOT L2
L5 STR

C≡C
1 2

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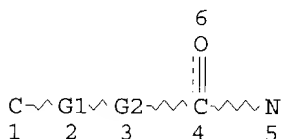
RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 2

STEREO ATTRIBUTES: NONE

L6 SCR 2039 OR 2041 OR 2050 OR 2049 OR 2048 OR 2053 OR 2052 O
R 2051 OR 2043

L7 STR



REP G1=(20-20) C

REP G2=(1-10) C

NODE ATTRIBUTES:

NSPEC IS RC AT 5

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 6

STEREO ATTRIBUTES: NONE

L8 1164 SEA FILE=REGISTRY SSS FUL (L7 AND L5) NOT L6

L9 STR

C≡C
1 2

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

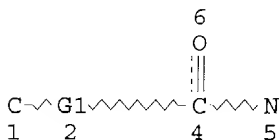
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NUMBER OF NODES IS 2

STEREO ATTRIBUTES: NONE

L10 SCR 2039 OR 2041 OR 2050 OR 2049 OR 2048 OR 2053 OR 2052 O
R 2051 OR 2043

L11 STR



REP G1=(5-9) C
 NODE ATTRIBUTES:
 NSPEC IS RC AT 5
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 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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 NUMBER OF NODES IS 5

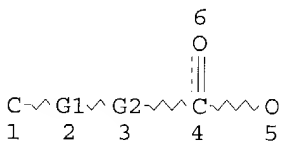
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 L12 25296 SEA FILE=REGISTRY SSS FUL (L11 AND L9) NOT L10
 L13 STR

C=C
 1 2

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 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 2

STEREO ATTRIBUTES: NONE
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 R 2051 OR 2043 OR 1838
 L15 STR



REP G1=(3-20) C
 REP G2=(0-10) C
 NODE ATTRIBUTES:
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 6

STEREO ATTRIBUTES: NONE
 L16 73850 SEA FILE=REGISTRY SSS FUL (L15 AND L13) NOT L14
 L17 STR

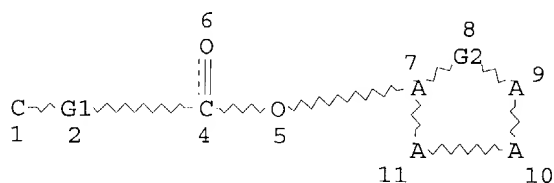
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 1 2

NODE ATTRIBUTES:
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 2

STEREO ATTRIBUTES: NONE

L18 SCR 2039 OR 2041 OR 2050 OR 2049 OR 2048 OR 2053 OR 2052 O
R 2051 OR 2043 OR 1840
L19 STR



REP G1=(5-9) C
REP G2=(0-4) A
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 10

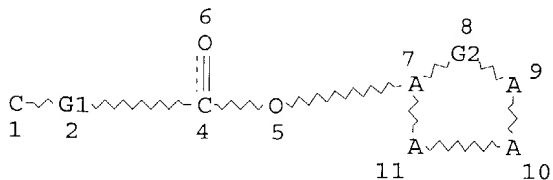
STEREO ATTRIBUTES: NONE
L20 2370 SEA FILE=REGISTRY SSS FUL (L19 AND L17) NOT L18
L21 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 2

STEREO ATTRIBUTES: NONE
L22 SCR 2039 OR 2041 OR 2050 OR 2049 OR 2048 OR 2053 OR 2052 O
R 2051 OR 2043 OR 1840
L23 STR

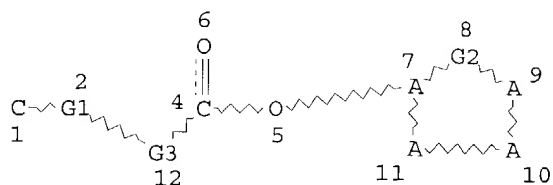


REP G1=(10-20) C
REP G2=(0-4) A
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE

L24 STR



```

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REP G2=(0-4) A
REP G3=(1-10) C
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

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GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 11

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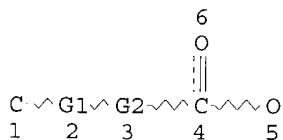
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STEREO ATTRIBUTES: NONE
L25      1058 SEA FILE=REGISTRY SSS FUL ((L24 OR L23) AND L21) NOT L22
L26      STR
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$$\begin{array}{c} \text{C} \equiv \text{C} \\ 1 \quad 2 \end{array}$$

NODE ATTRIBUTES:
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 2

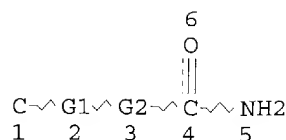
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STEREO ATTRIBUTES: NONE
L27          SCR 2039 OR 2041 OR 2050 OR 2049 OR 2048 OR 2053 OR 2052 O
R 2051 OR 2043
L28          STR
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```
REP G1=(3-20) C
REP G2=(0-10) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 6

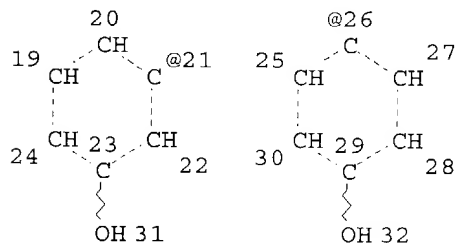
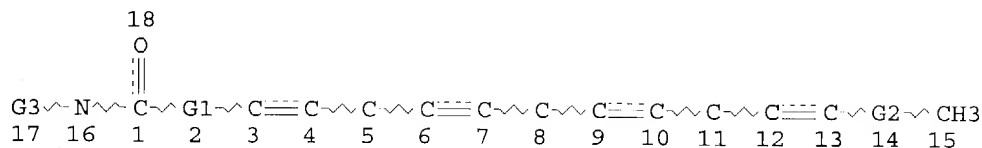
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STEREO ATTRIBUTES: NONE
L29      13336 SEA FILE=REGISTRY SSS FUL (L28 AND L26) NOT L27
L30      108806 SEA FILE=REGISTRY ABB=ON  PLU=ON  L4 OR L8 OR L12 OR L16 OR
          L20 OR L25 OR L29
L31      STR
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REP G1=(18-20) C
REP G2=(0-1) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 6

STEREO ATTRIBUTES: NONE
L33 STR



REP G1=(3-3) C
REP G2=(4-4) C
VAR G3=21/26
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 32

STEREO ATTRIBUTES: NONE

L34 83 SEA FILE=REGISTRY SUB=L30 SSS FUL L31 OR L33
L35 108723 SEA FILE=REGISTRY ABB=ON PLU=ON L30 NOT L34
L36 5 SEA FILE=REGISTRY ABB=ON PLU=ON ANANDAMIDE
L38 186720 SEA FILE=HCAPLUS ABB=ON PLU=ON L35
L39 1358 SEA FILE=HCAPLUS ABB=ON PLU=ON L36 OR ?ANANDAMID?
L43 70 SEA FILE=HCAPLUS ABB=ON PLU=ON INHIBIT? (L) TRANSPORT (L) L39
L44 62 SEA FILE=HCAPLUS ABB=ON PLU=ON L43 AND L38
L45 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L44 AND PD=<JUNE 9, 1999

=>
=>

=> d ibib abs hitstr l45 1-9

L45 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:510255 HCAPLUS

DOCUMENT NUMBER: 131:295096

TITLE: Unsaturated Long-Chain N-Acyl-vanillyl-amides
(N-AVAMs): Vanilloid Receptor Ligands That

**Inhibit Anandamide-Facilitated
Transport** and Bind to CB1 Cannabinoid
Receptors

AUTHOR(S): Melck, Dominique; Bisogno, Tiziana; De Petrocellis,
Luciano; Chuang, Huai-hu; Julius, David; Bifulco,
Maurizio; Di Marzo, Vincenzo

CORPORATE SOURCE: Istituto per la Chimica di Molecole di Interesse
Biologico, Consiglio Naz. Ric., Arco Felice, Napoli,
80072, Italy

SOURCE: Biochemical and Biophysical Research Communications (
1999), 262(1), 275-284
CODEN: BBRCA9; ISSN: 0006-291X

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We investigated the effect of changing the length and degree of unsatn. of the fatty acyl chain of N-(3-methoxy-4-hydroxy)-benzyl-cis-9-octadecenoamide (olvanil), a ligand of vanilloid receptors, on its capability to: (i) **inhibit anandamide-facilitated transport** into cells and enzymic hydrolysis, (ii) bind to CB1 and CB2 cannabinoid receptors, and (iii) activate the VR1 vanilloid receptor. Potent **inhibition** of [¹⁴C]**anandamide** accumulation into cells was achieved with C20:4 n-6, C18:3 n-6 and n-3, and C18:2 n-6 N-acyl-vanillyl-amides (N-AVAMs). The saturated analogs and Δ9-trans-olvanil were inactive. Activity in CB1 binding assays increased when increasing the number of cis-double bonds in a n-6 fatty acyl chain and, in saturated N-AVAMs, was not greatly sensitive to decreasing the chain length. The C20:4 n-6 analog (arvanil) was a potent **inhibitor of anandamide** accumulation (IC₅₀ = 3.6 μM) and was 4-fold more potent than **anandamide** on CB1 receptors (K_i = 0.25-0.52 μM), whereas the C18:3 n-3 N-AVAM was more selective than arvanil for the uptake (IC₅₀ = 8.0 μM) vs. CB1 receptors (K_i = 3.4 μM). None of the compds. efficiently **inhibited** [¹⁴C]**anandamide** hydrolysis or bound to CB2 receptors. All N-AVAMs activated the cation currents coupled to VR1 receptors overexpressed in Xenopus oocytes. In a simple, intact cell model of both vanilloid- and **anandamide**-like activity, i.e., the **inhibition** of human breast cancer cell (HBCC) proliferation, arvanil was shown to behave as a "hybrid" activator of cannabinoid and vanilloid receptors. (c) 1999 Academic Press.

IT **94421-68-8, Anandamide**

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

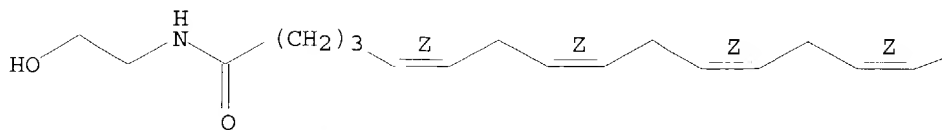
(unsatd. long-chain N-acyl-vanillyl-amides as vanilloid receptor ligands that **inhibit anandamide-facilitated transport** and bind to CB1 cannabinoid receptors)

RN 94421-68-8 HCAPLUS

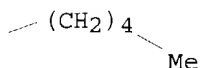
CN 5,8,11,14-Eicosatetraenamide, N-(2-hydroxyethyl)-, (5Z,8Z,11Z,14Z)- (9CI)
(CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



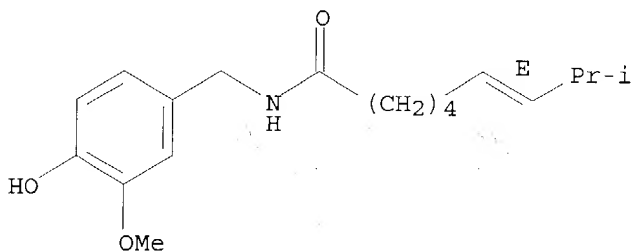
IT 404-86-4, Capsaicin 16729-47-8 58493-49-5,
Olvanil 95548-23-5 104899-01-6 104926-32-1
128007-31-8

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (unsatd. long-chain N-acyl-vanillyl-amides as vanilloid receptor ligands that **inhibit anandamide**-facilitated **transport** and bind to CB1 cannabinoid receptors)

RN 404-86-4 HCAPLUS

CN 6-Nonenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-8-methyl-, (6E) - (9CI) (CA INDEX NAME)

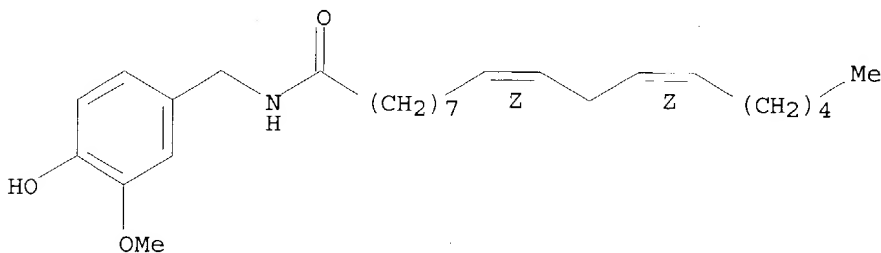
Double bond geometry as shown.



RN 16729-47-8 HCAPLUS

CN 9,12-Octadecadienamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (9Z,12Z) - (9CI) (CA INDEX NAME)

Double bond geometry as shown.

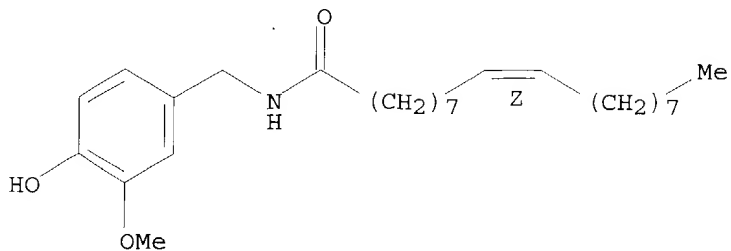


RN 58493-49-5 HCAPLUS

CN 9-Octadecenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (9Z) - (9CI) (CA

INDEX NAME)

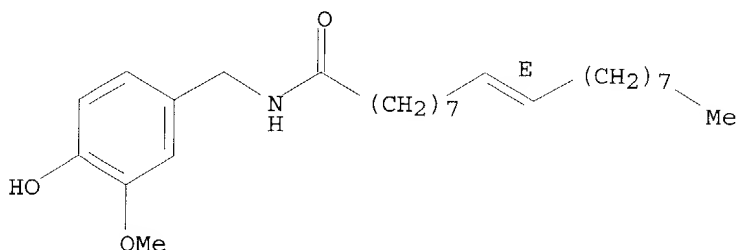
Double bond geometry as shown.



RN 95548-23-5 HCAPLUS

CN 9-Octadecenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (9E)- (9CI) (CA INDEX NAME)

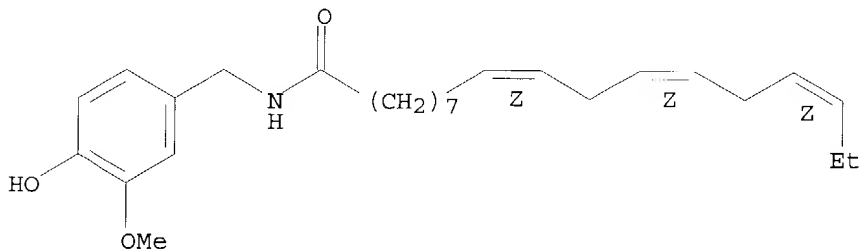
Double bond geometry as shown.



RN 104899-01-6 HCAPLUS

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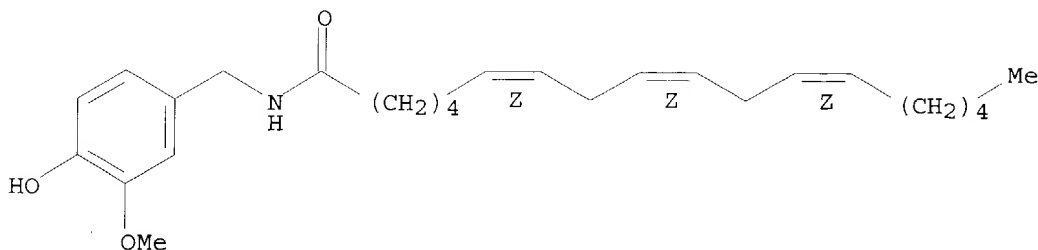
Double bond geometry as shown.



RN 104926-32-1 HCAPLUS

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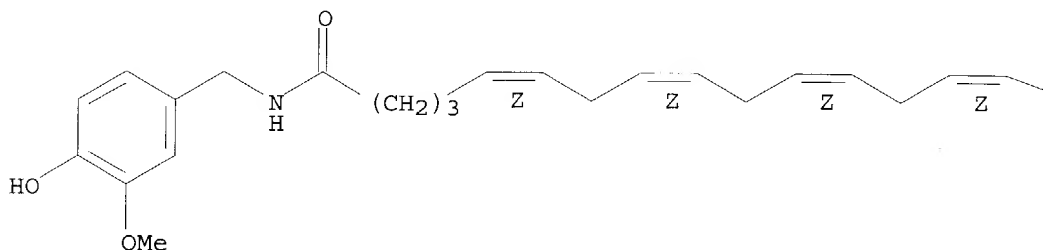
Double bond geometry as shown.



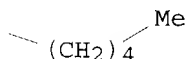
RN 128007-31-8 HCAPLUS
 CN 5,8,11,14-Eicosatetraenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-,
 (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1999:477642 HCAPLUS
 DOCUMENT NUMBER: 131:251951
 TITLE: Structure-activity relationships of anandamide, an endogenous cannabinoid ligand
 AUTHOR(S): Khanolkar, Atmaram D.; Makriyannis, Alexandros
 CORPORATE SOURCE: Departments of Pharmaceutical Sciences, University of Connecticut, Storrs, CT, 06269, USA
 SOURCE: Life Sciences (1999), 65(6/7), 607-616
 CODEN: LIFSAK; ISSN: 0024-3205
 PUBLISHER: Elsevier Science Inc.
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English

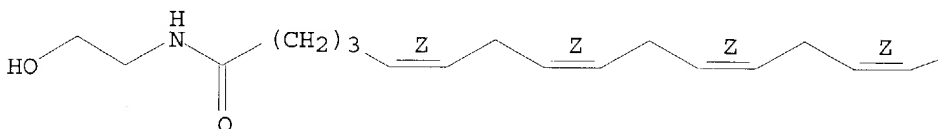
AB A review with 45 refs. Identification of arachidonylethanolamide (**anandamide**) as an endogenous cannabinoid is one of the most important developments in cannabinoid research in recent years. In a relatively short period of time thereafter, pharmacol. and biochem. studies have confirmed initial speculations that **anandamide** is a neuromodulator and significantly advanced our understanding of cannabinoid biochem. Moreover, the discovery of **anandamide** has led to the

identification of two heretofore unknown proteins associated with cannabinoid physiol.: (1) **Anandamide** Amidohydrolase (AAH), an enzyme responsible for the hydrolytic breakdown of **anandamide** and (2) the **Anandamide** Transporter (ANT), a carrier protein involved in the **transport** of **anandamide** across the cell membrane. Evidence obtained so far suggests that these two proteins, in combination, are responsible for the termination of the biol. actions of **anandamide**. Also, the discovery of **anandamide** has revealed a novel class of more selective cannabimimetic agents possessing a somewhat different pharmacol. profile of potential therapeutic value. A number of such analogs have now been reported many of which possess markedly improved cannabinoid receptor affinity and metabolic stability compared to those of the parent ligand. Generally, **anandamide** and all known analogs exhibit significant selectivity for the CB1 receptor and modest to very low affinity for CB2. For this reason, this group of compds. can be considered as CB1 ligands. The purpose of this review is to summarize the structure-activity relationships (SAR) of **anandamide** for the CB1 cannabinoid receptor and to define the structural requirements for the substrates and the **inhibitors** of **anandamide** amidohydrolase and the **anandamide** transporter.

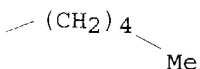
IT 94421-68-8, Anandamide
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (structure-activity relationships of anandamide, endogenous cannabinoid ligand)
 RN 94421-68-8 HCAPLUS
 CN 5,8,11,14-Eicosatetraenamide, N-(2-hydroxyethyl)-, (5Z,8Z,11Z,14Z)- (9CI)
 (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:314488 HCAPLUS

DOCUMENT NUMBER: 131:100242

TITLE: Structural determinants for recognition and translocation by the anandamide transporter

AUTHOR(S): Piomelli, D.; Beltramo, M.; Glasnapp, S.; Lin, S. Y.; Goutopoulos, A.; Xie, Xiang-Qun; Makriyannis, A.

CORPORATE SOURCE: The Neurosciences Institute, San Diego, CA, 92121, USA
 SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1999), 96(10), 5802-5807

CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The biol. actions of **anandamide** (arachidonylethanolamide), an endogenous cannabinoid lipid, are terminated by a two-step inactivation process consisting of carrier-mediated uptake and intracellular hydrolysis. **Anandamide** uptake in neurons and astrocytes is mediated by a high-affinity, Na⁺-independent transporter that is selectively **inhibited** by N-(4-hydroxyphenyl)-arachidonamide (AM404). In the present study, we examined the structural determinants governing recognition and translocation of substrates by the **anandamide** transporter constitutively expressed in a human astrocytoma cell line. Competition expts. with a select group of analogs suggest that substrate recognition by the transporter is favored by a polar nonionizable head group of defined stereochem. configuration containing a hydroxyl moiety at its distal end. The secondary carboxamide group interacts favorably with the transporter, but may be replaced with either a tertiary amide or an ester, suggesting that it may serve as hydrogen acceptor. Thus, 2-arachidonylglycerol, a putative endogenous cannabinoid ester, also may serve as a substrate for the transporter. Substrate recognition requires the presence of at least one cis double bond situated at the middle of the fatty acid carbon chain, indicating a preference for ligands whose hydrophobic tail can adopt a bent U-shaped conformation. On the other hand, uptake expts. with radioactively labeled substrates show that no fewer than four cis nonconjugated double bonds are required for optimal translocation across the cell membrane, suggesting that substrates are transported in a folded hairpin conformation. These results outline the general structural requisites for **anandamide transport** and may assist in the development of selective **inhibitors** with potential clin. applications.

IT 111-58-0 506-32-1 1808-26-0 2566-89-4

24257-12-3 35474-99-8 53847-30-6

94421-68-8 150314-34-4 156910-28-0

157182-49-5 157182-50-8 162758-93-2

162758-96-5 164228-51-7 166100-34-1

183718-67-4 187224-16-4 187224-18-6

213027-54-4 231632-70-5 231632-71-6

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231632-75-0 231632-76-1 231632-77-2

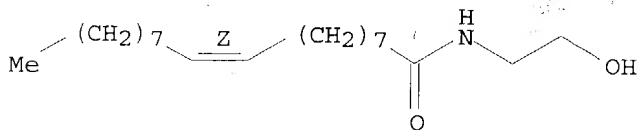
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

(structural determinants for recognition and translocation by the anandamide transporter)

RN 111-58-0 HCAPLUS

CN 9-Octadecenamide, N-(2-hydroxyethyl)-, (9Z)- (9CI) (CA INDEX NAME)

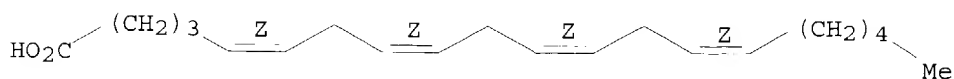
Double bond geometry as shown.



RN 506-32-1 HCAPLUS

CN 5,8,11,14-Eicosatetraenoic acid, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

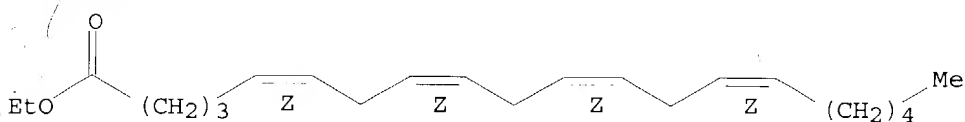
Double bond geometry as shown.



RN 1808-26-0 HCAPLUS

CN 5,8,11,14-Eicosatetraenoic acid, ethyl ester, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

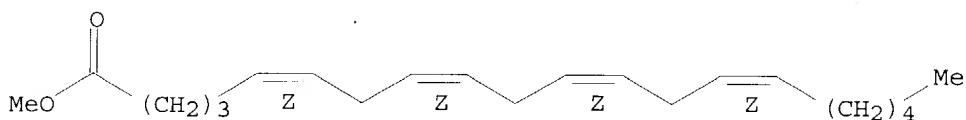
Double bond geometry as shown.



RN 2566-89-4 HCAPLUS

CN 5,8,11,14-Eicosatetraenoic acid, methyl ester, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

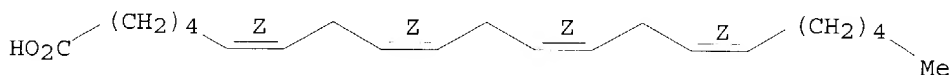
Double bond geometry as shown.



RN 24257-12-3 HCAPLUS

CN 6,9,12,15-Heneicosatetraenoic acid, (6Z,9Z,12Z,15Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

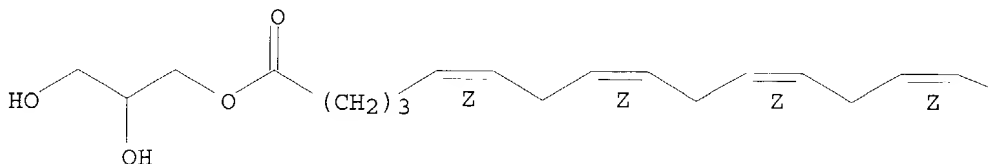


RN 35474-99-8 HCAPLUS

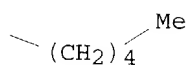
CN 5,8,11,14-Eicosatetraenoic acid, 2,3-dihydroxypropyl ester, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A

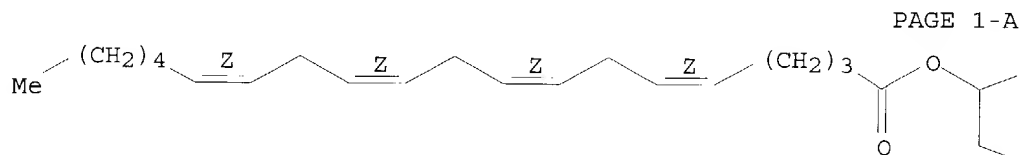


PAGE 1-B



RN 53847-30-6 HCAPLUS
 CN 5,8,11,14-Eicosatetraenoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester,
 (5Z,8Z,11Z,14Z) - (9CI) (CA INDEX NAME)

Double bond geometry as shown.



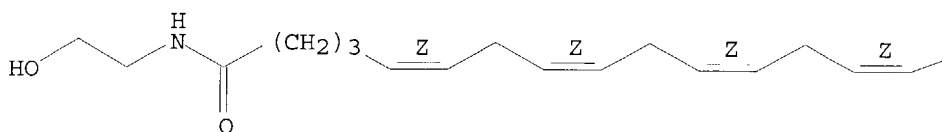
PAGE 1-A

PAGE 1-B



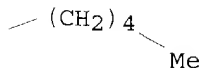
RN 94421-68-8 HCAPLUS
 CN 5,8,11,14-Eicosatetraenamide, N-(2-hydroxyethyl) -, (5Z,8Z,11Z,14Z) - (9CI)
 (CA INDEX NAME)

Double bond geometry as shown.



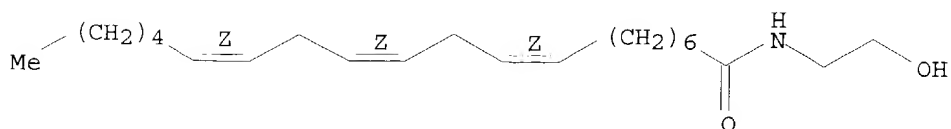
PAGE 1-A

PAGE 1-B



RN 150314-34-4 HCAPLUS
 CN 8,11,14-Eicosatrienamide, N-(2-hydroxyethyl) -, (8Z,11Z,14Z) - (9CI) (CA
 INDEX NAME)

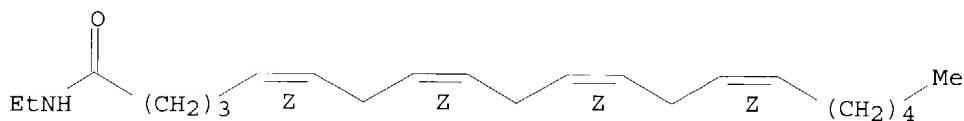
Double bond geometry as shown.



RN 156910-28-0 HCAPLUS

CN 5,8,11,14-Eicosatetraenamide, N-ethyl-, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



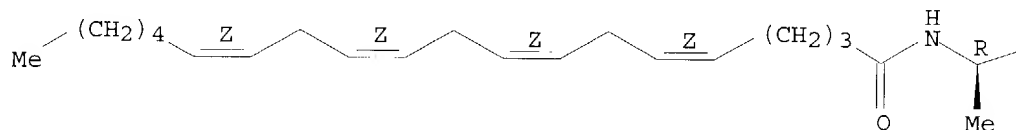
RN 157182-49-5 HCAPLUS

CN 5,8,11,14-Eicosatetraenamide, N-[(1R)-2-hydroxy-1-methylethyl]-, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

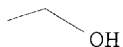
Absolute stereochemistry. Rotation (+).

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



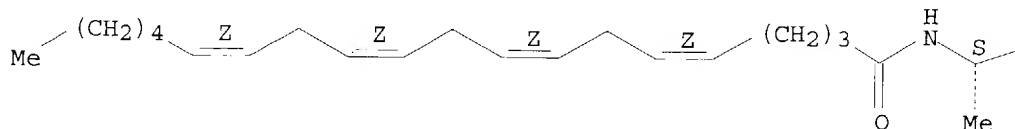
RN 157182-50-8 HCAPLUS

CN 5,8,11,14-Eicosatetraenamide, N-[(1S)-2-hydroxy-1-methylethyl]-, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A

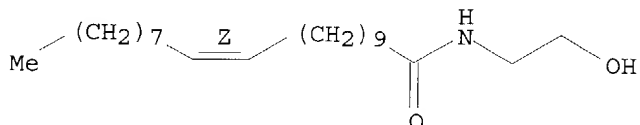


PAGE 1-B



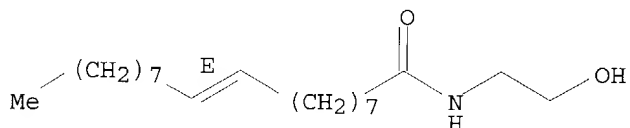
RN 162758-93-2 HCAPLUS
CN 11-Eicosenamide, N-(2-hydroxyethyl)-, (11Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



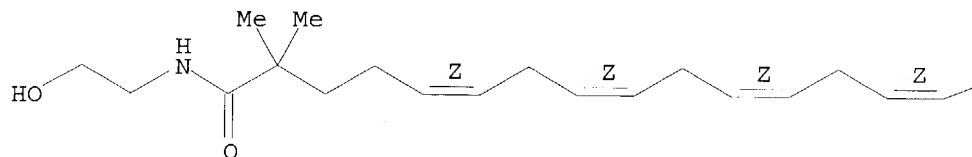
RN 162758-96-5 HCAPLUS
CN 9-Octadecenamide, N-(2-hydroxyethyl)-, (9E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



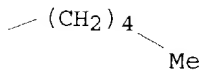
RN 164228-51-7 HCAPLUS
CN 5,8,11,14-Eicosatetraenamide, N-(2-hydroxyethyl)-2,2-dimethyl-,
(5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



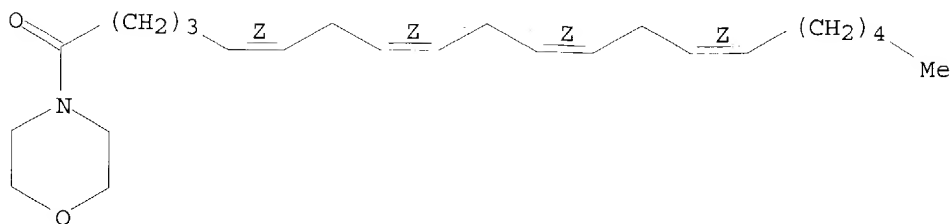
PAGE 1-A

PAGE 1-B



RN 166100-34-1 HCAPLUS
CN Morpholine, 4-[(5Z,8Z,11Z,14Z)-1-oxo-5,8,11,14-eicosatetraenyl]- (9CI)
(CA INDEX NAME)

Double bond geometry as shown.

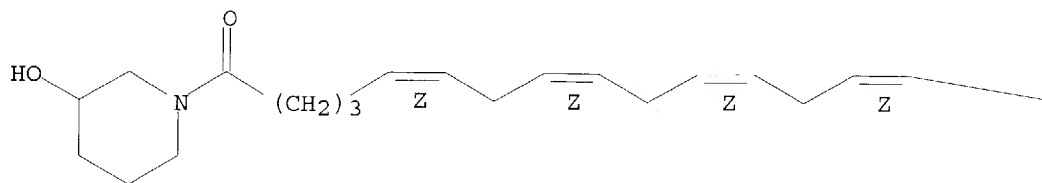


RN 183718-67-4 HCAPLUS

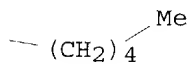
CN 3-Piperidinol, 1-[(5Z,8Z,11Z,14Z)-1-oxo-5,8,11,14-eicosatetraenyl]- (9CI)
(CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

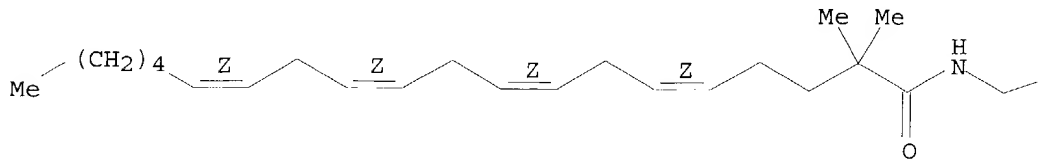


RN 187224-16-4 HCAPLUS

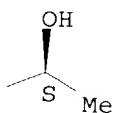
CN 5,8,11,14-Eicosatetraenamide, N-[(2S)-2-hydroxypropyl]-2,2-dimethyl-,
(5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



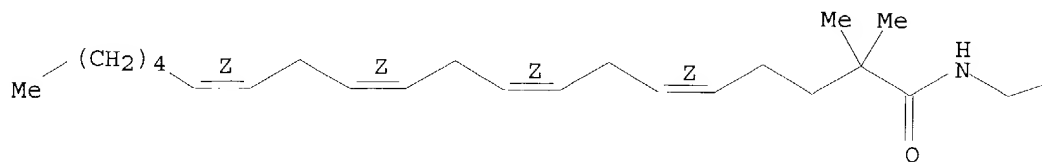
RN 187224-18-6 HCAPLUS

CN 5,8,11,14-Eicosatetraenamide, N-[(2R)-2-hydroxypropyl]-2,2-dimethyl-,

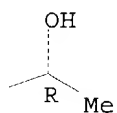
(5Z,8Z,11Z,14Z) - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

PAGE 1-A



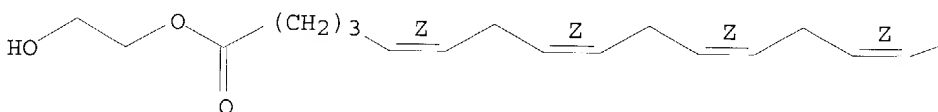
PAGE 1-B



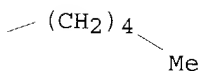
RN 213027-54-4 HCAPLUS
CN 5,8,11,14-Eicosatetraenoic acid, 2-hydroxyethyl ester, (5Z,8Z,11Z,14Z) - (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A

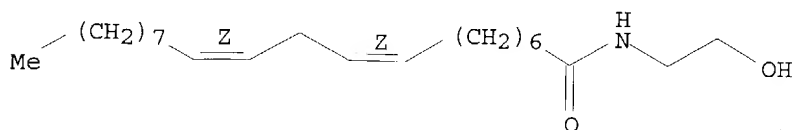


PAGE 1-B

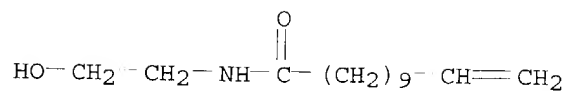


RN 231632-70-5 HCAPLUS
CN 8,11-Eicosadienamide, N-(2-hydroxyethyl) -, (8Z,11Z) - (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 231632-71-6 HCAPLUS
CN 11-Dodecenamide, N-(2-hydroxyethyl) - (9CI) (CA INDEX NAME)

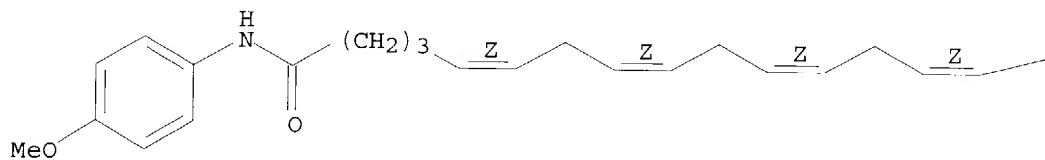


RN 231632-72-7 HCAPLUS

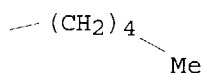
CN 5,8,11,14-Eicosatetraenamide, N-(4-methoxyphenyl)-, (5Z,8Z,11Z,14Z)- (9CI)
(CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

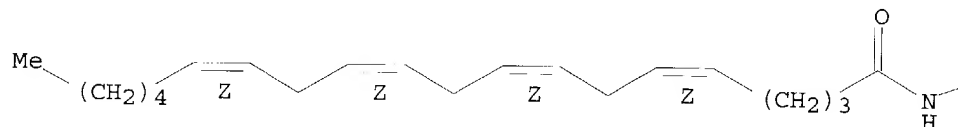


RN 231632-73-8 HCAPLUS

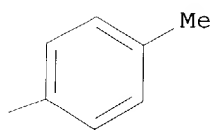
CN 5,8,11,14-Eicosatetraenamide, N-(4-methylphenyl)-, (5Z,8Z,11Z,14Z)- (9CI)
(CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

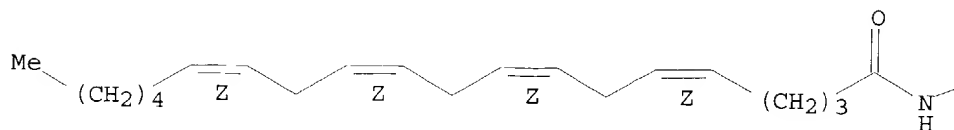


RN 231632-74-9 HCAPLUS

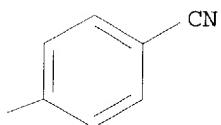
CN 5,8,11,14-Eicosatetraenamide, N-(4-cyanophenyl)-, (5Z,8Z,11Z,14Z)- (9CI)
(CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



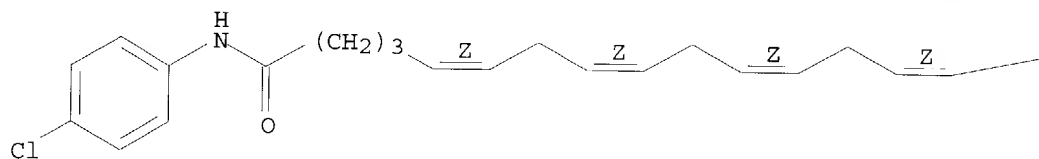
PAGE 1-B



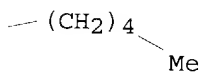
RN 231632-75-0 HCAPLUS
 CN 5,8,11,14-Eicosatetraenamide, N-(4-chlorophenyl)-, (5Z,8Z,11Z,14Z)- (9CI)
 (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



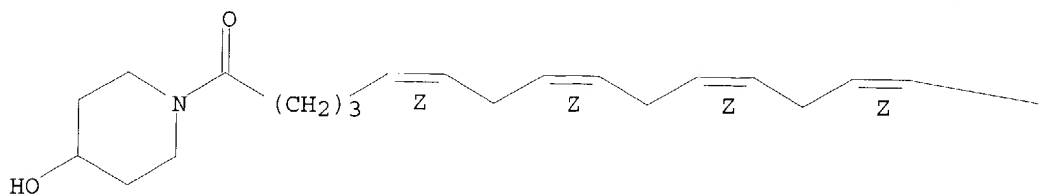
PAGE 1-B



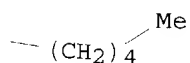
RN 231632-76-1 HCAPLUS
 CN 4-Piperidinol, 1-[(5Z,8Z,11Z,14Z)-1-oxo-5,8,11,14-eicosatetraenyl]- (9CI)
 (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A

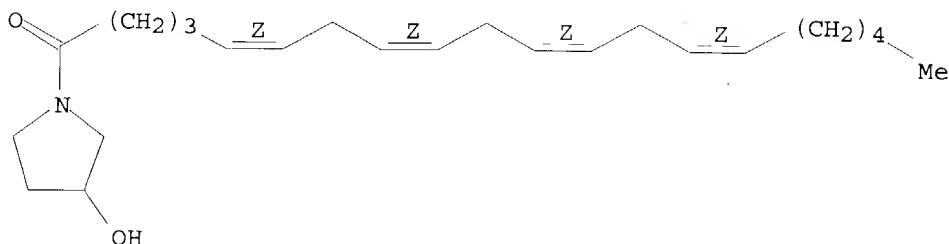


PAGE 1-B



RN 231632-77-2 HCAPLUS
 CN 3-Pyrrolidinol, 1-[(5Z,8Z,11Z,14Z)-1-oxo-5,8,11,14-eicosatetraenyl]- (9CI)
 (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:811082 HCAPLUS

DOCUMENT NUMBER: 130:218085

TITLE: **Anandamide transport**

inhibition by the vanilloid agonist olvanil

Beltramo, Massimiliano; Piomelli, Daniele

CORPORATE SOURCE: The Neurosciences Institute, San Diego, CA, 92121, USA

SOURCE: European Journal of Pharmacology (1999),

364(1), 75-78

CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The structural similarities between the **anandamide transport inhibitor** N-(4-hydroxyphenyl)-arachidonamide (AM404) and the synthetic vanilloid agonist olvanil [(N-vanillyl)-9-oleamide], prompted us to investigate the possibility that olvanil may interfere with **anandamide transport**. The intracellular accumulation of [3H]**anandamide** by human astrocytoma cells was prevented by olvanil with a K_i value of 14.1 ± 7.1 μ M. By contrast, capsaicin [(8-methyl-N-vanillyl)-6-nonenamide], a plant-derived vanilloid agonist, and capsazepine (N-[2-(4-chlorophenyl)ethyl]-1,3,4,5-tetrahydro-7,8-dihydroxy-2H-2-benzazepine-2-carboxamide), a vanilloid antagonist, had no such effect ($K_i > 100$ μ M). These results indicate that, although less potent than AM404 (K_i 2.1 ± 0.2 μ M), olvanil may reduce **anandamide** clearance at concns. similar to those needed for vanilloid receptor activation.

IT **404-86-4**, Capsaicin **58493-49-5**, Olvanil

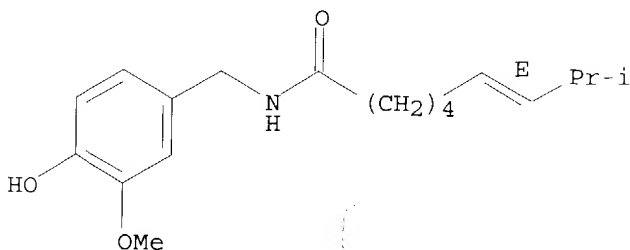
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**anandamide transport inhibition** by vanilloid agonist olvanil)

RN 404-86-4 HCAPLUS

CN 6-Nonenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-8-methyl-, (6E) - (9CI)
(CA INDEX NAME)

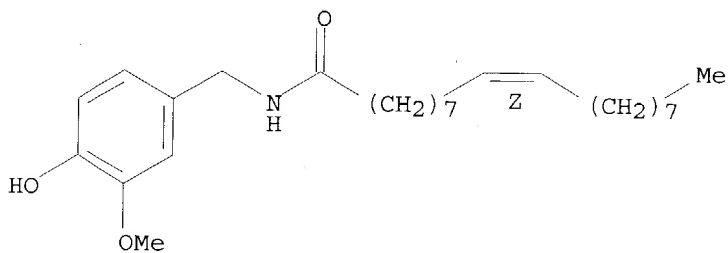
Double bond geometry as shown.



RN 58493-49-5 HCAPLUS

CN 9-Octadecenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (9Z) - (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT 94421-68-8, Anandamide

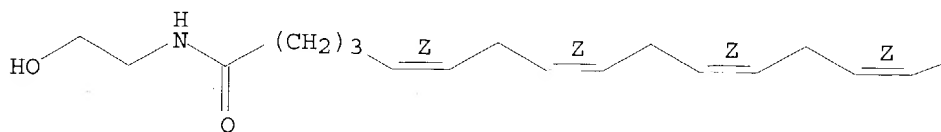
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(anandamide transport inhibition by vanilloid agonist olvanil)

RN 94421-68-8 HCAPLUS

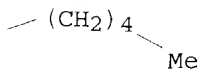
CN 5,8,11,14-Eicosatetraenamide, N-(2-hydroxyethyl)-, (5Z,8Z,11Z,14Z) - (9CI)
(CA INDEX NAME)

Double bond geometry as shown.



PAGE 1-A

PAGE 1-B



REFERENCE COUNT:

21

THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:698015 HCAPLUS

DOCUMENT NUMBER: 130:76092

TITLE: Interactions between synthetic vanilloids and the endogenous cannabinoid system

AUTHOR(S): Di Marzo, Vincenzo; Bisogno, Tiziana; Melck, Dominique; Ross, Ruth; Brockie, Heather; Stevenson, Lesley; Pertwee, Roger; De Petrocellis, Luciano
CORPORATE SOURCE: Istituto per la Chimica di Molecole di Interesse Biologico, CNR, Arco Felice, 80072, Italy

SOURCE: FEBS Letters (1998), 436(3), 449-454

CODEN: FEBLAL; ISSN: 0014-5793

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The chemical similarity between some synthetic agonists of vanilloid receptors, such as olvanil (N-vanillyl-cis-9-octadecenoamide), and the 'endocannabinoid' **anandamide** (arachidonoyl-ethanolamide, AEA), suggests possible interactions between the cannabinoid and vanilloid signalling systems. Here the authors report that olvanil is a stable and potent **inhibitor** of AEA facilitated **transport** into rat basophilic leukemia (RBL-2H3) cells. Olvanil blocked both the uptake and the hydrolysis of [14C]AEA by intact RBL-2H3 cells (IC₅₀ = 9 μM), while capsaicin and pseudocapsaicin (N-vanillyl-nonanamide) were much less active. Olvanil was more potent than previously reported **inhibitors** of AEA facilitated **transport**, i.e. phloretin (IC₅₀ = 80 μM), AM404 (12.9%, **inhibition** at 10 μM) or oleoylethanolamide (27.5% **inhibition** at 10 μM). Olvanil was a poor **inhibitor** of [14C]AEA hydrolysis by RBL-2H3 and N18TG2 cell membranes, suggesting that the **inhibitory** effect on [14C]AEA breakdown observed in intact cells was due to **inhibition** of [14C]AEA uptake. Olvanil was stable to enzymic hydrolysis, and (i) displaced the binding of high affinity cannabinoid receptor ligands to membrane preps. from N18TG2 cells and guinea pig forebrain (K_i = 1.64-7.08 μM), but not from cells expressing the CB2 cannabinoid receptor subtype; (ii) **inhibited** forskolin-induced cAMP formation in intact N18TG2 cells (IC₅₀ = 1.60 μM), this effect being reversed by the selective CB1 antagonist SR141716A. Pseudocapsaicin, but not capsaicin, also selectively bound to CB1 receptor-containing membranes. These data suggest that some of the analgesic actions of olvanil may be due to its interactions with the endogenous cannabinoid system, and may lead to the design of a novel class of cannabimimetics with potential therapeutic applications as analgesics.

IT 111-58-0 404-86-4, Capsaicin 58493-49-5,

Olvanil 94421-68-8, Anandamide

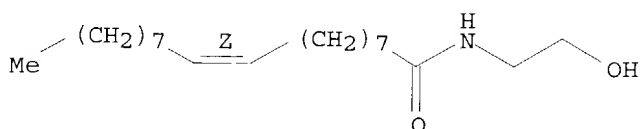
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(interactions between synthetic vanilloids and the endogenous cannabinoid system)

RN 111-58-0 HCAPLUS

CN 9-Octadecenamide, N-(2-hydroxyethyl)-, (9Z)- (9CI) (CA INDEX NAME)

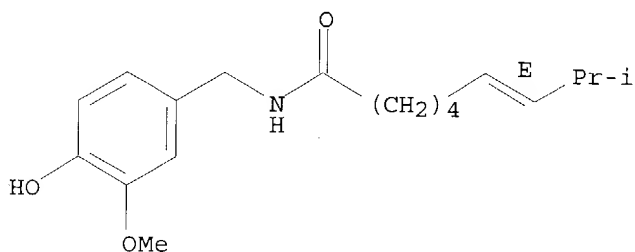
Double bond geometry as shown.



RN 404-86-4 HCAPLUS

CN 6-Nonenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-8-methyl-, (6E)-(9CI)
(CA INDEX NAME)

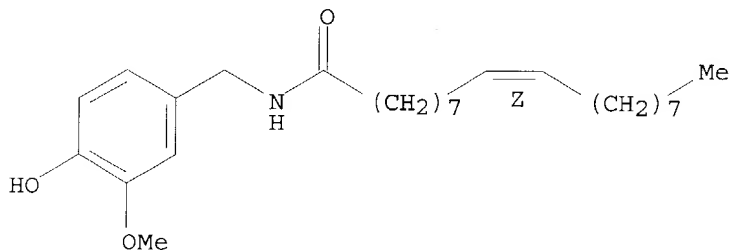
Double bond geometry as shown.



RN 58493-49-5 HCAPLUS

CN 9-Octadecenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (9Z)-(9CI) (CA INDEX NAME)

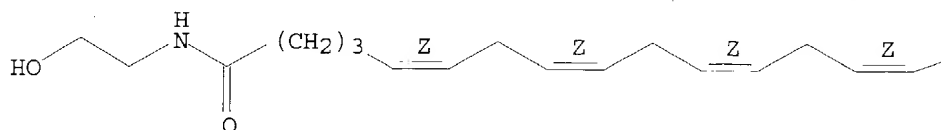
Double bond geometry as shown.



RN 94421-68-8 HCAPLUS

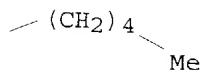
CN 5,8,11,14-Eicosatetraenamide, N-(2-hydroxyethyl)-, (5Z,8Z,11Z,14Z)-(9CI)
(CA INDEX NAME)

Double bond geometry as shown.



PAGE 1-A

PAGE 1-B



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:808015 HCAPLUS

DOCUMENT NUMBER: 128:136686

TITLE: Inhibition of intestinal motility by anandamide, an endogenous cannabinoid

AUTHOR(S): Calignano, Antonio; La Rana, Giovanna; Makriyannis, Alexandros; Lin, Sun Y.; Beltramo, Massimiliano; Piomelli, Daniele

CORPORATE SOURCE: Department of Experimental Pharmacology, University of Naples, Naples 80123, Italy

SOURCE: European Journal of Pharmacology (1997), 340(2/3), R7-R8

CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The endogenous cannabinoid ligand **anandamide** (arachidonylethanolamide) **inhibited** the intestinal passage of a charcoal meal when administered s.c. in mice at doses ranging from 0.1 to 50 mg/kg. This effect was prevented by the cannabinoid CB1 receptor antagonist SR141716A [N-(piperidin-1-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-1H-pyrazole-3-carboxamide·HCl] (1 mg/kg s.c.), but it was not affected by the **anandamide transport inhibitor**, N-(4-hydroxyphenyl) arachidonylethanolamide (AM404) (50 mg/kg, s.c.). The results indicate that **anandamide** modulates intestinal motility in mice by activating cannabinoid CB1 receptors. They also suggest that **anandamide transport**, which was previously shown to participate in terminating neural and vascular responses to **anandamide**, does not contribute to **anandamide** inactivation in intestinal tissue.

IT 94421-68-8, Anandamide

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

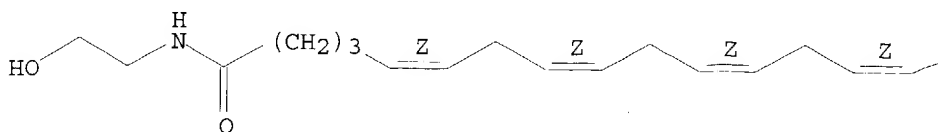
(intestinal motility inhibition by anandamide mediation by cannabinoid receptors)

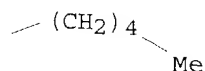
RN 94421-68-8 HCAPLUS

CN 5,8,11,14-Eicosatetraenamide, N-(2-hydroxyethyl)-, (5Z,8Z,11Z,14Z)- (9CI)
(CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A





REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:646587 HCAPLUS

DOCUMENT NUMBER: 127:329390

TITLE: Potentiation of **anandamide** hypotension by the **transport inhibitor**, AM404

AUTHOR(S): Calignano, Antonio; La Rana, Giovanna; Beltramo, Massimiliano; Makriyannis, Alexandros; Piomelli, Daniele

CORPORATE SOURCE: Department of Experimental Pharmacology, University of Naples, Naples, 80123, Italy

SOURCE: European Journal of Pharmacology (1997), 337(1), R1-R2

CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The putative endogenous cannabinoid, **anandamide** (0.2-2 mg/kg i.v.), decreased systemic blood pressure dose-dependently in anesthetized guinea pigs. These effects were prevented by the CB1 cannabinoid receptor antagonist SR141716A [N-(piperidin-1-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-1H-pyrazole-3-carboxamide·HCl] at the dose of 0.2 mg/kg i.v. The vasodepressor responses to **anandamide** were significantly potentiated and prolonged by a novel **inhibitor** of carrier-mediated **anandamide transport**, N-(4-hydroxyphenyl) arachidonylethanolamide (AM404) (10 mg/kg, i.v.). These results suggest that **anandamide transport** participates in terminating the vascular actions of **anandamide**.

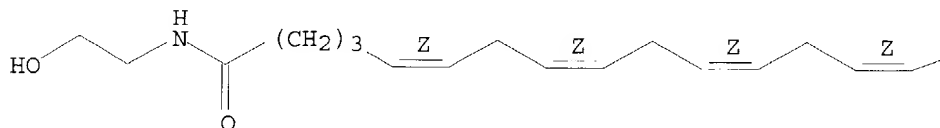
IT 94421-68-8, **Anandamide**

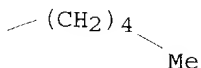
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(potentiation of **anandamide** hypotension by **transport inhibitor**, AM404)

RN 94421-68-8 HCAPLUS

CN 5,8,11,14-Eicosatetraenamide, N-(2-hydroxyethyl)-, (5Z,8Z,11Z,14Z)- (9CI)
(CA INDEX NAME)

Double bond geometry as shown.





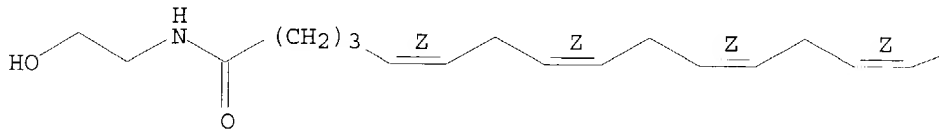
L45 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1997:550217 HCAPLUS
 DOCUMENT NUMBER: 127:246072
 TITLE: Functional role of high-affinity **anandamide transport**, as revealed by selective **inhibition**
 AUTHOR(S): Beltramo, M.; Stella, N.; Calignano, A.; Lin, S. Y.; Makriyannis, A.; Piomelli, D.
 CORPORATE SOURCE: The Neurosciences Inst., San Diego, CA, 92121, USA
 SOURCE: Science (Washington, D. C.) (1997), 277(5329), 1094-1097
 CODEN: SCIEAS; ISSN: 0036-8075
 PUBLISHER: American Association for the Advancement of Science
 DOCUMENT TYPE: Journal
 LANGUAGE: English

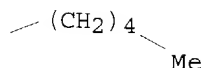
AB **Anandamide**, an endogenous ligand for central cannabinoid receptors, is released from neurons on depolarization and rapidly inactivated. **Anandamide** inactivation is not completely understood, but it may occur by **transport** into cells or by enzymic hydrolysis. The compound N-(4-hydroxyphenyl)arachidonamide (AM404) was shown to **inhibit** high-affinity **anandamide** accumulation in rat neurons and astrocytes in vitro, an indication that this accumulation resulted from carrier-mediated **transport**. Although AM404 did not activate cannabinoid receptors or **inhibit anandamide** hydrolysis, it enhanced receptor-mediated **anandamide** responses in vitro and in vivo. The data indicate that carrier-mediated **transport** may be essential for termination of the biol. effects of **anandamide**, and may represent a potential drug target.

IT **94421-68-8**, Anandamide
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (carrier-mediated transport of anandamide)

RN 94421-68-8 HCAPLUS
 CN 5,8,11,14-Eicosatetraenamide, N-(2-hydroxyethyl)-, (5Z,8Z,11Z,14Z)- (9CI)
 (CA INDEX NAME)

Double bond geometry as shown.





L45 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:495779 HCAPLUS

DOCUMENT NUMBER: 127:188622

TITLE: Accumulation of N-arachidonoyl ethanolamine (anandamide) into cerebellar granule cells occurs via facilitated diffusion

AUTHOR(S): Hillard, Cecilia J.; Edgemond, William S.; Jarrahan, Abbas; Campbell, William B.

CORPORATE SOURCE: Department of Pharmacology and Toxicology, Medical College of Wisconsin, Milwaukee, WI, 53226, USA

SOURCE: Journal of Neurochemistry (1997), 69(2), 631-638

CODEN: JONRA9; ISSN: 0022-3042

PUBLISHER: Lippincott-Raven

DOCUMENT TYPE: Journal

LANGUAGE: English

AB N-Arachidonoyl ethanolamine (anandamide, AEA) is a putative endogenous ligand of the cannabinoid receptor. Intact cerebellar granule neurons in primary culture rapidly accumulate AEA. [3H]AEA accumulation by cerebellar granule cells is dependent on incubation time ($t_{1/2}$ of 2.6 ± 0.8 min at 37°C) and temperature. The accumulation of AEA is saturable and has an apparent K_m of 41 ± 15 μM and a V_{max} of 0.61 ± 0.04 nmol/min/106 cells. [3H]AEA accumulation by cerebellar granule cells is significantly reduced by 200 μM phloretin ($57.4 \pm 4\%$ of control) in a noncompetitive manner. [3H]AEA accumulation is not **inhibited** by either ouabain or removal of extracellular sodium. [3H]AEA accumulation is fairly selective for AEA among other naturally occurring N-acyl ethanolamines; only N-oleoyl ethanolamine significantly **inhibited** [3H]AEA accumulation at a concentration of 10 μM . The ethanolamides of palmitic acid and linolenic acid were inactive at 10 μM . N-Arachidonoyl benzylamine and N-arachidonoyl propylamine, but not arachidonic acid, 15-hydroxy-AEA, or 12-hydroxy-AEA, compete for AEA accumulation. When cells are preloaded with [3H]AEA, temperature-dependent efflux occurs with a half-life of 1.9 ± 1.0 min. Phloretin does not **inhibit** [3H]AEA efflux from cells. These results suggest that AEA is accumulated by cerebellar granule cells by a protein-mediated **transport** process that has the characteristics of facilitated diffusion.

IT 94421-68-8, Anandamide

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

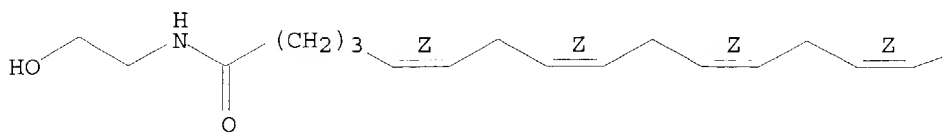
(accumulation of N-arachidonoyl ethanolamine into cerebellar granule cells occurs via facilitated diffusion)

RN 94421-68-8 HCAPLUS

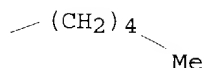
CN 5,8,11,14-Eicosatetraenamide, N-(2-hydroxyethyl)-, (5Z,8Z,11Z,14Z)- (9CI)
(CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



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R 2051 OR 2043
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 L44 62 SEA FILE=HCAPLUS ABB=ON PLU=ON L43 AND L38
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 L46 1 SEA FILE=REGISTRY ABB=ON PLU=ON ARACHIDONOYLETHAN/BI
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L52 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:735737 HCAPLUS

DOCUMENT NUMBER: 132:62244

TITLE: The endothelial component of cannabinoid-induced relaxation in rabbit mesenteric artery depends on gap junctional communication

AUTHOR(S): Chaytor, A. T.; Martin, P. E. M.; Evans, W. H.; Randall, M. D.; Griffith, T. M.

CORPORATE SOURCE: Departments of Diagnostic Radiology and Cardiovascular Sciences Research Group, University of Wales College of Medicine, Cardiff, CF4 4XN, UK

SOURCE: Journal of Physiology (Cambridge, United Kingdom) (1999), 520(2), 539-550

CODEN: JPHYA7; ISSN: 0022-3751

PUBLISHER: Cambridge University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 1. The authors have shown that the endocannabinoid **anandamide** and its stable analog methanandamide relax rings of rabbit superior mesenteric artery through endothelium-dependent and -independent mechanisms that are unaffected by blockade of NO synthase and cyclooxygenase. 2. The endothelium-dependent component of the responses was attenuated by the gap junction **inhibitor** 18 α -glycyrrhetic acid (18 α -GA; 50 μ M), and a synthetic connexin-mimetic peptide homologous to the extracellular Gap 27 sequence of connexin 43 (43Gap 27, SRPTEKTIFII; 300 μ M). By contrast, the corresponding connexin 40 peptide (40Gap 27, SRPTEKNVFIV) was inactive. 3. The cannabinoid CB1 receptor antagonist SR141716A (10 μ M) also attenuated endothelium-dependent relaxations but this **inhibition** was not observed with the CB1 receptor antagonist LY320135 (10 μ M). Furthermore, SR141716A mimicked the effects of 43Gap 27 peptide in blocking Lucifer Yellow dye transfer between coupled COS-7 cells (a monkey fibroblast cell line), whereas LY320135 was without effect, thus suggesting that the action of SR141716A was directly attributable to effects on gap junctions. 4. The endothelium-dependent component of cannabinoid-induced relaxation was also attenuated by AM404 (10 μ M), an **inhibitor** of the high-affinity **anandamide transporter**, which was without effect on dye transfer. 5. Taken together, the findings suggest that cannabinoids derived from arachidonic acid gain access to the endothelial cytosol via a **transporter** mechanism and subsequently stimulate relaxation by promoting diffusion of

an endothelium-derived hyperpolarizing factor to adjacent smooth muscle cells via gap junctions. 6. Relaxations of endothelium-denuded preps. to **anandamide** and methanandamide were unaffected by 43Gap 27 peptide, 18 α -GA, SR141716A, AM404 and indomethacin and their genesis remains to be established.

IT 94421-68-8, Anandamide 150314-39-9

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

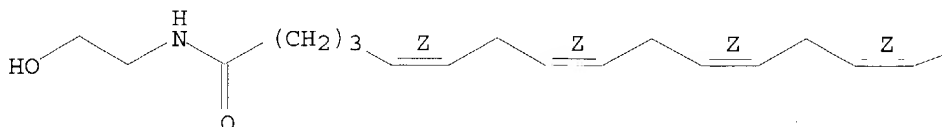
(endothelial component of cannabinoid-induced relaxation in rabbit mesenteric artery depends on gap junctional communication and not on CB1 receptors)

RN 94421-68-8 HCAPLUS

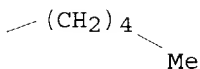
CN 5,8,11,14-Eicosatetraenamide, N-(2-hydroxyethyl)-, (5Z,8Z,11Z,14Z)- (9CI)
(CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

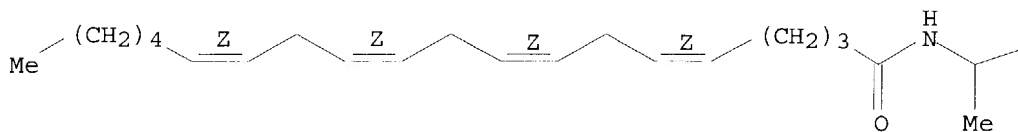


RN 150314-39-9 HCAPLUS

CN 5,8,11,14-Eicosatetraenamide, N-(2-hydroxy-1-methylethyl)-, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:262822 HCAPLUS

DOCUMENT NUMBER: 131:71734

TITLE: Anandamide activates human platelets through a pathway independent of the arachidonate cascade

AUTHOR(S): Maccarrone, Mauro; Bari, Monica; Menichelli, Adriana;
 CORPORATE SOURCE: Del Principe, Domenico; Finazzi Agro, Alessandro
 SOURCE: Department of Experimental Medicine and Biochemical
 Sciences, University of Rome Tor Vergata, Rome,
 I-00133, Italy
 PUBLISHER: FEBS Letters (1999), 447(2,3), 277-282
 CODEN: FEBLAL; ISSN: 0014-5793
 DOCUMENT TYPE: Elsevier Science B.V.
 LANGUAGE: Journal
 English

AB **Anandamide (arachidonoyl ethanolamide, AnNH)** is shown
 to activate human platelets, a process which was not **inhibited**
 by acetylsalicylic acid (aspirin). Unlike AnNH, hydroperoxides generated
 thereof by lipoxygenase activity, and the congener (13-
 hydroxy)linoleoyl ethanolamide, were unable to activate platelets, though
 they counteracted AnNH-mediated stimulation. On the other hand,
 palmitoyl ethanolamide neither activated human platelets nor blocked the
 AnNH effects. AnNH inactivation by human platelets was afforded by a
 high-affinity **transporter**, which was activated by nitric
 oxide-donors up to 225% of the control. The internalized AnNH could thus
 be hydrolyzed by a fatty acid amide hydrolase (FAAH), characterized here
 for the first time.

IT **94421-68-8, Anandamide**
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological
 process); BSU (Biological study, unclassified); BIOL (Biological study);
 PROC (Process)

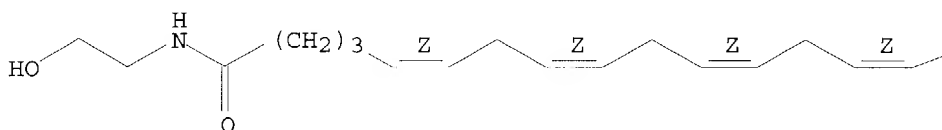
(anandamide activates human platelets through a pathway independent of
 arachidonate cascade)

RN 94421-68-8 HCAPLUS

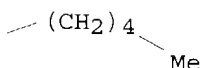
CN 5,8,11,14-Eicosatetraenamide, N-(2-hydroxyethyl)-, (5Z,8Z,11Z,14Z)- (9CI)
 (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

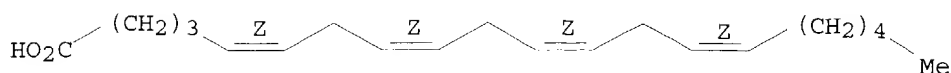


IT **506-32-1, Arachidonic acid 219931-42-7**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); BIOL (Biological study)
 (anandamide activates human platelets through a pathway independent of
 arachidonate cascade)

RN 506-32-1 HCAPLUS

CN 5,8,11,14-Eicosatetraenoic acid, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

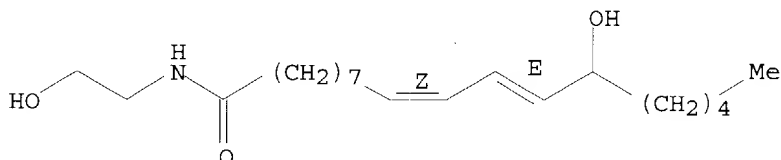
Double bond geometry as shown.



RN 219931-42-7 HCAPLUS

CN 9,11-Octadecadienamide, 13-hydroxy-N-(2-hydroxyethyl)-, (9Z,11E)- (9CI)
(CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L52 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:783697 HCAPLUS

DOCUMENT NUMBER: 130:122662

TITLE: Anandamide hydrolysis by human cells in culture and brain

AUTHOR(S): Maccarrone, Mauro; Van Der Stelt, Marcelis; Rossi, Antonello; Veldink, Gerrit A.; Vliegenthart, Johannes F. G.; Agro, Alessandro Finazzi

CORPORATE SOURCE: Department of Experimental Medicine and Biochemical Sciences, University of Rome Tor Vergata, Rome, I-00133, Italy

SOURCE: Journal of Biological Chemistry (1998), 273(48), 32332-32339

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

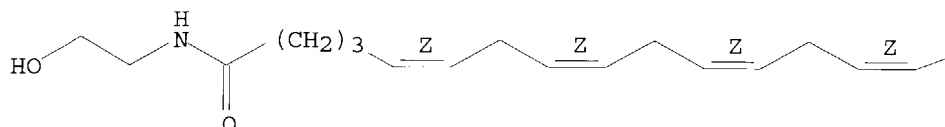
AB **Anandamide (arachidonylethanolamide; AnNH)** has important neuromodulatory and immunomodulatory activities. This lipid is rapidly taken up and hydrolyzed to arachidonate and ethanolamine in many organisms. As yet, AnNH inactivation has not been studied in humans. Here, a human brain fatty-acid amide hydrolase (FAAH) has been characterized as a single protein of 67 kDa with a pI of 7.6, showing apparent K_m and V_{max} values for AnNH of $2.0 \pm 0.2 \mu M$ and $800 \pm 75 \text{ pmol} \cdot \text{min}^{-1} \cdot \text{mg}$ of protein $^{-1}$, resp. The optimum pH and temperature for AnNH hydrolysis were 9.0 and 37 °C, resp., and the activation energy of the reaction was $43.5 \pm 4.5 \text{ kJ} \cdot \text{mol}^{-1}$. Hydro(pero)xides derived from AnNH or its linoleoyl analogs by lipoxygenase action were competitive **inhibitors** of human brain FAAH, with apparent K_i values in the low micromolar range. One of these compds., linoleoylethanolamide is the first natural **inhibitor** ($K_i = 9.0 \pm 0.9 \mu M$) of FAAH as yet discovered. An FAAH activity sharing several biochem. properties with the human brain enzyme was demonstrated in human neuroblastoma CHP100 and lymphoma U937 cells. Both cell lines have a high affinity **transporter** for AnNH, which had apparent K_m and V_{max} values for AnNH of $0.20 \pm 0.02 \mu M$ and $30 \pm 3 \text{ pmol} \cdot \text{min}^{-1} \cdot \text{mg}$ of protein $^{-1}$ (CHP100 cells) and $0.13 \pm 0.01 \mu M$ and $140 \pm 15 \text{ pmol} \cdot \text{min}^{-1} \cdot \text{mg}$ of protein $^{-1}$ (U937

cells), resp. The AnNH carrier of both cell lines was activated up to 170% of the control by nitric oxide.

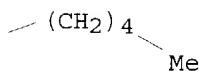
IT **94421-68-8**, Anandamide
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (anandamide hydrolysis by human cells in culture and brain)
 RN 94421-68-8 HCAPLUS
 CN 5,8,11,14-Eicosatetraenamide, N-(2-hydroxyethyl)-, (5Z,8Z,11Z,14Z)- (9CI)
 (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A

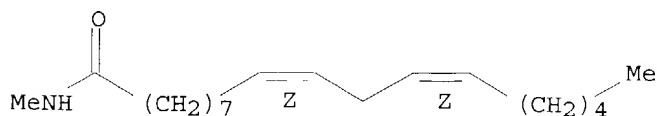


PAGE 1-B



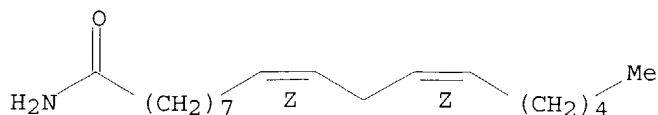
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171627-25-1 171756-49-3 219931-40-5
219931-41-6 219931-42-7 219931-43-8
219931-44-9
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (in brain fatty-acid amide hydrolase inhibition and anandamide hydrolysis by human cells in culture and brain)
 RN 3140-44-1 HCAPLUS
 CN 9,12-Octadecadienamide, N-methyl-, (9Z,12Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



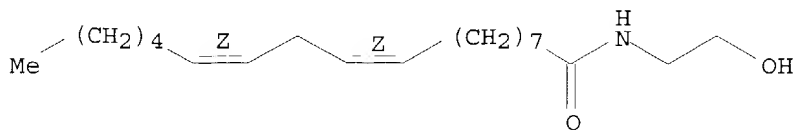
RN 3999-01-7 HCAPLUS
 CN 9,12-Octadecadienamide, (9Z,12Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 68171-52-8 HCAPLUS
 CN 9,12-Octadecadienamide, N-(2-hydroxyethyl)-, (9Z,12Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

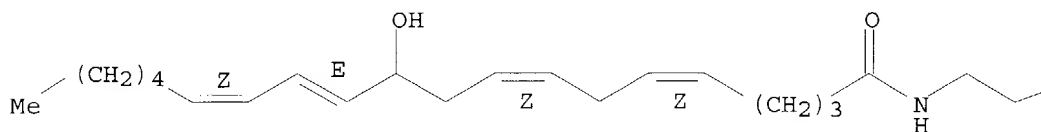


RN 171627-25-1 HCAPLUS

CN 5,8,12,14-Eicosatetraenamide, 11-hydroxy-N-(2-hydroxyethyl)-,
(5Z,8Z,12E,14Z) - (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

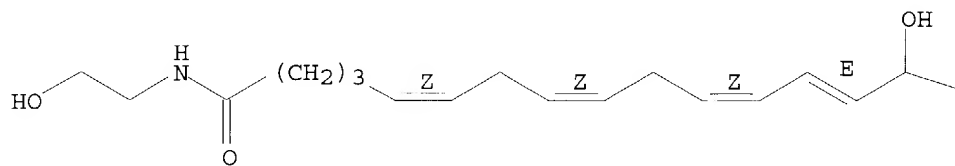
OH

RN 171756-49-3 HCAPLUS

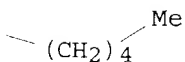
CN 5,8,11,13-Eicosatetraenamide, 15-hydroxy-N-(2-hydroxyethyl)-,
(5Z,8Z,11Z,13E) - (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

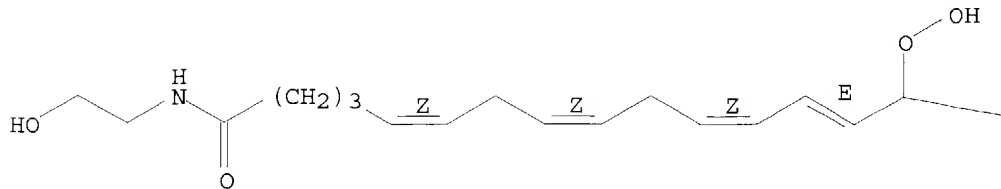


RN 219931-40-5 HCAPLUS

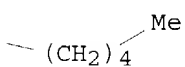
CN 5,8,11,13-Eicosatetraenamide, 15-hydroperoxy-N-(2-hydroxyethyl)-,
(5Z,8Z,11Z,13E) - (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

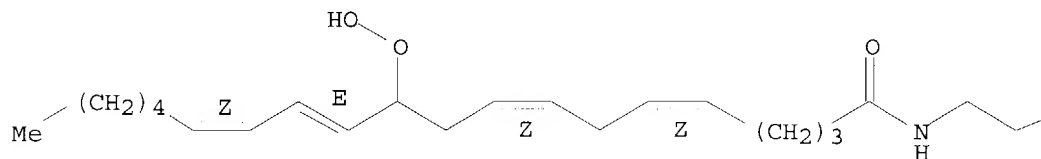


RN 219931-41-6 HCAPLUS

CN 5,8,12,14-Eicosatetraenamide, 11-hydroperoxy-N-(2-hydroxyethyl)-,
(5Z,8Z,12E,14Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



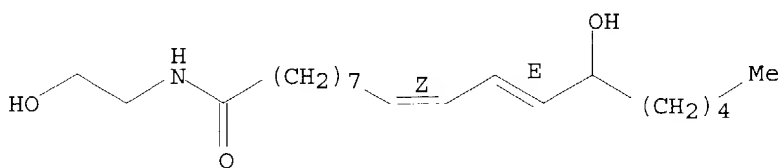
PAGE 1-B



RN 219931-42-7 HCAPLUS

CN 9,11-Octadecadienamide, 13-hydroxy-N-(2-hydroxyethyl)-, (9Z,11E)- (9CI)
(CA INDEX NAME)

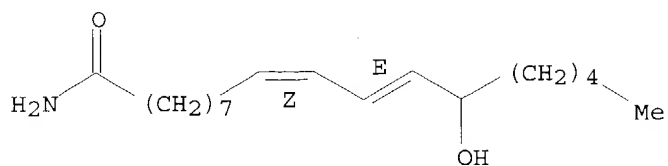
Double bond geometry as shown.



RN 219931-43-8 HCAPLUS

CN 9,11-Octadecadienamide, 13-hydroxy-, (9Z,11E)- (9CI) (CA INDEX NAME)

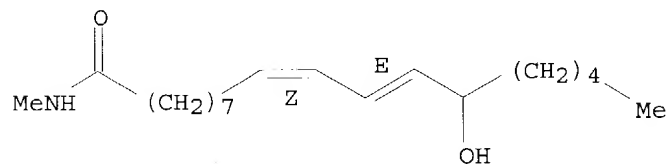
Double bond geometry as shown.



RN 219931-44-9 HCAPLUS

CN 9,11-Octadecadienamide, 13-hydroxy-N-methyl-, (9Z,11E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT:

46

THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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